

REMARKS

Further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 48-71 are pending in the application. Claims 48-71 are under consideration and stand rejected.

Provisional Rejections

Applicants have noted that claims 48-71 have been provisionally rejected as unpatentable over claims of U.S. Patent Application No. 11/335,196 and U.S. Patent Application No. 11/375,818. Applicants maintain that the rejections are not proper. Applicants will take appropriate action in the event that either of the rejections mature; however applicants note that both U.S. Patent Application No. 11/335,196 and U.S. Patent Application No. 11/375,818 are indicated by PAIR as being abandoned.

Rejection under 35 U.S.C. § 112

Claim 63 has been rejected under 35 U.S.C. § 112 as being indefinite for allegedly lacking antecedent basis for "said step of digesting." That limitation is found in claim 49, from which claim 63 ultimately depends through a series of intervening claims. Accordingly, applicants submit that the step is supported and has adequate antecedent basis. Reconsideration and withdrawal are respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 48-71 have been rejected under 35 U.S.C. § 102 as allegedly anticipated by Gunderson (USPA 20030207295; USSN 10/264,574). Applicants traverse the rejection. The

Gunderson '574 application does not describe or disclose each and every step of the rejected claims. Accordingly, the rejection is improper and should be withdrawn.

The Gunderson '574 application is presently involved in Interference No. 105,547 with Applicants' U.S. Patent No. 6,858,412 ("the '412 patent"). Applicants refer the Examiner to the record in Interference No. 105,547, wherein Gunderson argued that its application disclosed inventions claimed in the '412 patent. As in the interference, the Gunderson '574 application fails to disclose applicants' claimed invention.

In order to provoke that interference, Gunderson copied claims from applicants' '412 patent into the '574 application on September 26, 2005. Specifically, Gunderson's claims 23-24 are verbatim copies of applicants' claims 1 and 37 from the '412 patent. Gunderson's claim 25 encompasses the same method as claims 23-24, but was cobbled together using terminology taken out of context from the specification of the '574 application. As Gunderson's claims were copied from applicant's '412 patent, it should not be assumed that those claims are supported by the Gunderson specification as originally filed. In fact, the copied claims are not supported by the Gunderson '574 application. In the interference, Applicants have shown that Gunderson's '574 application does not describe the methods recited in the copied claims, because the Gunderson '574 application describes fundamentally different processes than were claimed in Applicants' '512 patent.

As in the claims in the '412 patent in interference, the instant claims recite a process wherein a closed circular probe is formed, the circular probe is cleaved, the cleaved probe is amplified, and then the amplicons of the amplified cleaved closed circular probe are detected. The Gunderson '574 application does not disclose the presently claimed methods. In particular, the Gunderson '574 application fails to provide supporting disclosure for, among other things, cleavage of a closed circular probe, amplification of the resulting cleaved

probes, or detection of amplicons of the cleaved probe in a process such as that of the instant claims.

Claim 48 as currently presented recites:

A method of detecting one or more nucleic acid target sequences in a sample, the method comprising the steps of:

forming one or more closed circular probes whenever a first targeting domain and a second targeting domain of any of a plurality of precircle probes hybridize with their respective first target domains and second target domains of the one or more target sequences such that 5' and 3' nucleotides of the respective precircle probes abut one another, each precircle probe further having at least a first universal primer site and a cleavage site;

cleaving the one or more closed circular probes to form cleaved probes;

amplifying cleaved probes using a first universal primer complementary with a first universal primer site to form one or more amplicons; and

detecting the amplicons to detect the one or more nucleic acid target sequences in the sample.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The elements must be arranged as required by the claim. *In re Bond*, 910 F.2d 831, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990).

The Examiner has not shown that the Gunderson '574 application discloses every element of the presently claimed methods. On page 6 of the Office Action, the Examiner has indicated paragraphs of the '574 application that are alleged to describe the formation of a closed circular probe, amplification of a probe using a universal primer, and detection of amplicon. Notably absent is any indication of a paragraph in the Gunderson '574 application that is even alleged to disclose the step "cleaving the one or more closed circular probes to form cleaved probes." The Gunderson '574 application does not even suggest such a step. Consequently, none of the paragraphs referenced as allegedly disclosing the subsequent steps

actually refer to amplification of cleaved probes or detection of amplicons produced by amplifying the cleaved probe.

Gunderson only describes amplifying a closed circular probe by rolling circle amplification (RCA). By its nature, RCA requires a closed circular probe, and cannot be performed on a cleaved circular probe.

The only cleavage described by Gunderson in a method using a closed circular probe is cleaving the product of the rolling circle amplification (RCA). The product of RCA is a linear DNA. Thus, cleavage of the product of RCA cannot be confused with a step corresponding to *cleaving a closed circular probe*. See, e.g., Gunderson '574, para. 0182 ("Thus, in a preferred embodiment the OLA/RCA is performed in solution followed by restriction endonuclease cleavage of the RCA product." emphasis added); see also Fig. 6 and para. 0064 (illustrating OLA/RCA and the single stranded linear product of amplification of the probe (58)).

Cleavage of the linear product of an RCA process is not cleavage of a closed circular probe. No such step is cited or identified in the outstanding rejection. Accordingly, the rejection fails to support a *prima facie* case of anticipation, and the rejection should be withdrawn.

Similarly, applicants reject any notion that the circular probe of the RCA process is inherently cleaved by the process described by Gunderson. In order for a disclosure to be inherent, the missing descriptive matter must necessarily be present in the specification such that one of skill in the art would have recognized such a disclosure. Further, to provide "inherent" support for an affirmative limitation (e.g., cleaving a closed circular probe), the "inherent limitation must be the 'necessary and only reasonable construction' to be given the

disclosure by one skilled in the art." *Langer and Tornqvist v. Kaufman and McMullen*, 175 USPQ 172, 174 (CCPA 1972) citations omitted.

Cleavage of the RCA amplification product as described by Gunderson would not necessarily result in cleavage of the original probe, and thus would not inherently comprise a cleavage step as that step is recited in the instant claims. There has been no showing to the contrary. Therefore, cleavage of a closed circular probe is not an inherent property of the methods disclosed by Gunderson.

Furthermore, since there is no teaching or suggestion of cleaving a closed circular probe in any method taught by Gunderson, there cannot be any teaching or suggestion of the steps that follow cleaving the closed circular probe in the present claims, in which the cleaved probe is amplified and detected. Each of the steps of the present claims recites action upon the product of the preceding step so that any anticipating disclosure would have to disclose such steps performed in the sequence recited.

Any disclosure alleged to anticipate claim 48 and its dependent claims would have to, at least, disclose amplifying cleaved probes produced by cleaving closed circular probes. The paragraphs of the Gunderson '574 application related to amplification that have been cited in the outstanding rejection do not teach or suggest amplifying cleaved probes produced by cleaving closed circular probes.

Any disclosure alleged to anticipate claim 48 and its dependent claims would have to, at least, disclose a method comprising detection of amplicons produced by amplifying a cleaved circular probe. The paragraphs and original claims of the Gunderson '574 application related to detection of amplicons that have been cited in the outstanding rejection do not teach or suggest detection of amplicons produced by amplifying a cleaved circular probe.

For at least the foregoing reasons, the Gunderson '574 application does not disclose every element of the instant claims, either explicitly or inherently, and so it could not have anticipated the instant claims. Reconsideration and withdrawal of that rejection are respectfully requested.

Rejections under 35 U.S.C. § 103

Claim 55 has been rejected under 35 U.S.C. § 103 as allegedly unpatentable over the Gunderson '574 application in view of Carter et al. (1971). The rejection is traversed.

The prior art fails to establish a proper prima facie case of obviousness. To establish a prima facie case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2143.

The rejection of claim 55 relies upon Gunderson as allegedly teaching all the elements of the claims from which claim 55 depends and digesting using exonucleases. Carter has been cited only for allegedly teaching denaturing an exonuclease. Carter et al. does not remedy the deficiencies of Gunderson that have been shown above. Thus, Gunderson and Carter et al., taken together, do not teach or suggest all the elements of claim 55. Accordingly, reconsideration and withdrawal of the rejection of claim 55 are respectfully requested.

CONCLUSION

In view of the above remarks and amendments, Applicants respectfully submit that the application is in condition for allowance. If the Examiner believes that a telephone call would be useful in expediting the allowance of the application, the Examiner is invited to contact the undersigned.

This response is accompanied by a request for a two month extension of time. Please charge the extension fee and any other fee that may be due to our Deposit Account No. 50-3655, under Order No. AFFY-201-102.

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Respectfully submitted,

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